AMENDMENTS TO THE SPECIFICATION

IN THE SPECIFICATION

On page 8, line 13, please replace the original paragraph with the following amended paragraph:

-- Preferably, the amino acid sequence is N V S V S V (SEQ ID NO: 2). This has been identified by the inventors as being a targeting signal. --

On page 9, line 8, please replace the original paragraph with the following amended paragraph:

-- Preferably m = 4-20, especially 5 to 10, and n =0 or 1, especially 1. Preferably Xaa_1 is not N V S V S V (SEQ ID NO: 2). Most preferably Xaa_2 is Y or A, especially A.--

On page 10, line 1, please replace the original paragraph with the following amended paragraph:

-- Preferably, the nucleotide sequence which is modified is contained within a nucleotide sequence encoding the sequence (SEQ ID NO: 5): --

On page 11, line 5, please replace the original paragraph with the following amended paragraph:

-- Preferably, the targeting signal is N V S V S V(SEQ ID NO: 2). --

On page 11, line 37, please replace the original paragraph with the following amended paragraph:

-- Preferred synthetic tailpieces formed by such sequences include:

(a) SCMVGHEALPMNFTQKTIDRLSGKPACY(SEQ ID NO: 7)

(b) SCMVGHEALPMNFTQKTIDRLSGKPAAACY(SEQ ID NO: 8)

(c) SCMVGHEALPMNFTQKTIDRLSGKPHASTPEPDPVACY(SEQ ID NO: 9)

and

(d) SCMVGHEALPMNFTQKTIDRLSGKPAAAAACY(SEQ ID NO: 69) ---

On page 12, line 6, please replace the original paragraph with the following amended paragraph:

-- Modifying the C-terminal end still further to include PAAAAACY (SEQ ID NO: 22) at the C-terminus produced an improvement in antibody secretion. --

On page 12, line 9, please replace the original paragraph with the following amended paragraph:

-- Further improvement is expected by removing the C-terminal tyrosine residue and optionally replacing it with Alanine. The terminal tyrosine is expected to be a potential vacuolar targeting signal. Frigerio, L., *et al.* (The Plant Cell, Vol. 10 (1998), pages 1031-1042) looked at phaseolin, a legume protein in plants. Deletion of four C-terminal residues (Ala Phe Val Tyr) (SEQ ID NO: 70) was found to prevent vacuolar targeting. Unpublished results by the authors of this paper also found that at least 50% of the vacuolar targeting was due to the C-terminal tyrosine residue. ---

On page 12, line 22, please replace the original paragraph with the following amended paragraph:

-- Hence, more preferably the antibody comprises a C-terminus sequence selected from:

-PAAAAACA(SEQ ID NO: 71) and

-PAAAAAC(SEQ ID NO: 72). --

On page 12, line 35, please replace the original paragraph with the following amended paragraph:

-- Oligonucleotides for use in the manufacture of the antibodies of the invention are also provided. These include : 5'-ccatcgatggaatggacctgggttttt-3'(SEQ ID NO: 10), 5'-ccctctagactagtagcataggccatc-3'(SEQ ID NO: 11), 5'-actgtagacaattccgccacctcagcctaca-3'(SEQ ID NO: 12), 5'-tgtaggctgaggtggcggaattgtctac agt-3'(SEQ ID NO: 13), 5'-gagcagctcaacagcgttttccgctcagtcag-3'(SEQ ID NO: 14), 5'-ctgactgagcggaaaacgctgttgagctgctc-3'(SEQ ID NO: 15), 5'-ttgcccatga acttcgtccagaagaccatcga-3'(SEQ ID NO: 16), 5'-tcgatggtcttctggacgaagttcatgggcaa-3'(SEQ ID NO: 17), 5'-aaacccaccaatgtcgctgt gtctgtgatcatg-3'(SEQ ID NO: 18), 5'-catgatcacagacacagcgacattggtgggttt-3'(SEQ ID NO: 19), 5'-aaacccaccaatgtcgctgt gtctgtgatcatg-3'(SEQ ID NO: 18), 5'-catgatcacagacacagcgacattggtgggttt-3'(SEQ ID NO: 19), 5'-ccctctagactatttacccgacagacggtc-3'(SEQ ID NO: 20), 5'-gagcagctca acagcgttttccgctcagtcag-3'(SEQ ID NO: 21). --

On page 14, line 38, please replace the original paragraph with the following amended paragraph:

-- Figure 8. Sequence homology of the C-terminus ends of IgA and IgM heavy chains (SEQ ID NOS: 25-68). --

On page 15, line 1, please replace the original paragraph with the following amended paragraph:

-- Figure 9. An artificial C-terminal tail PAAAAACY(SEQ ID NO: 22) allows J chain binding and dIgA/G ennamer assembly.

Tobacco protoplasts were transfected with plasmids encoding k chain and γ/α, γ/α ΔC18 or γ/α ΔC18P $(A)_5$CY(SEQ ID NO: 22) heavy chains, respectively, either in the presence or in the absence of plasmid encoding the J chain. Cells were pulse labelled for 1 h. Cell homogenates were immunoprecipitated with anti IgG antiserum. To analyse their assembly state, proteins were resolved by non-reducing SDS-PAGE and visualised by fluorography. Note that the efficiency of ennamer assembly of P$(A)_5$CY(SEQ ID NO: 22) is comparable to the wild-type IgA/G. ΔC18 is incapable of binding the J chain as it lacks the C-terminal cysteine. --

On page 15, line 11, please replace the original paragraph with the following amended paragraph:

-- Figure 10. The artificial P$(A)_5$CY(SEQ ID NO: 22) tail allows for improved antibody secretion.

Tobacco protoplasts were transfected with plasmids encoding k chain, J chain and γ/α, γ/α ΔC18 or γ/α ΔC18P$(A)_5$CY(SEQ ID NO: 22) heavy chains. Cells were pulse labelled for 1 h and chased for the indicated periods of time. Cell homogenates and incubation media were immunoprecipitated with anti IgG antiserum. Proteins were visualised by reducing SDS-PAGE and fluorography. The fluorograms were subjected to densitometry to quantify the amount of secreted heavy chains. Secreted heavy chains are expressed as percentage of total intracellular heavy chains immunoselected at 0 h chase. Note that at 8 hours, recovery of P$(A)_5$CY(SEQ ID NO: 22) in the medium is 2. 3-fold higher than recovery of IgA/G. --

On page 15, line 30, please replace the original paragraph with the following amended paragraph:

-- All DNA manipulations were performed using established procedures.

The full length IgA/G g/a heavy chain was amplified from the binary vector pMON530 using the polymerase chain reaction. The oligonucleotides 5'-ccatcgatggaatggacctgggttttt-3'(SEQ ID NO: 10) and 5'-ccctctagactagtagcataggccatc-3'(SEQ ID NO: 11) containing ClaI and XbaI restriction sites before the start codon and after the stop codon for cloning purposes, were used. The digested PCR products were ligated into a pUC-based vector downstream of the CaMV35S-promoter (Denecke et al. , 1992). The resulting plasmid was designated pJLH38. --

On page 16, line 1, please replace the original paragraph with the following amended paragraph:

-- The glycosylation site mutations were produced using the 'Quickchange' in vitro mutagenesis system (Stratagene, La Jolla, CA). Potential glycan sites mutations Ser 76 to Ala (Dglycanl pJLH40), Thr 289 to Val(Dglycan2 pJLH41), Thr 526 to Ala (Dglycan3 pJLH42) and Ser 541 to Ala (Dglycan4 pJLH43) were introduced using the oligonucleotides 5'-actgtagacaattccgccacctcagcctaca-3 (SEQ ID NO:12)', 5'-tgtaggctgaggtggcggaattgtctacagt-3'(SEQ ID NO: 13), 5'-gagcagctcaacagcgttttccgctcagtcag-3'(SEQ ID NO: 14), 5'-ctgactgagcggaaaacgctgttgagctgctc-3'(SEQ ID NO: 15), 5'-ttgcccatgaacttcgtccagaagaccatcga-3'(SEQ ID NO: 16), 5'-tcgatggtcttctggacgaagttcatgggcaa-3'(SEQ ID NO: 17), 5'-aaacccaccaatgtcgctgtgtctgtgatcatg-3'(SEQ ID NO: 18) or 5'-catgatcacagacacagcgacatt ggtgggttt-3'(SEQ ID NO: 19) respectively, using pJLH38 as a template. Multiple glycan mutants D3,4 was also produced using Quickchange in vitro mutagenesis system (Stratagene, La Jolla, CA) with the oligonucleotides 5'-aaacccaccaatgtcgctgtgtctgtgatcatg-3'(SEQ ID NO: 18) and5'-catgatcacagacacagcgacatt ggtgggttt-3'(SEQ ID NO: 19) and pJLH42 as template. The glycan mutant pJLH45, containing no glycosylation sites (D1, 2,3, 4) was produced by isolating the ClaI-NcoI fragment from pJLH40, the NcoI-EcoRI fragmentpJLH41,EcoRI-XbaI fragment from pJLH44 and ligating them into the pUC vector previously cut with ClaI and XbaI. Removal of the last 18 amino acids of the g/a heavy chain(DC18 pJLH47) was achieved by PCR using the anti-sense oligonucleotide 5'-ccctctagactatttacccgacagacggtc-3'(SEQ ID NO: 20) producing a stop codon followed by an Xbal site at position537 with the sense oligo 5'-gagcag ctcaacagcgttttccgctcagtcag-3'(SEQ ID NO: 21). The resulting PCR product was cut with EcoRI and XbaI and ligated into the expression vector cut with ClaI and XbaI along with a ClaI-EcoRI fragment ofpJLH38.

Phaseolin expression constructs T343F and D418 are described in Pedrazzini et al. (1997) and Frigerio et al. (1998), respectively. --

On page 24, line 24, please replace the original paragraph with the following amended paragraph:

-- The inventors have noted that deletion of the C-terminal end of the heavy chains of IgA and IgM results in deletion of the C-terminal cysteine residue responsible for J-chain binding. The presence of the J-chain increases peptidase resistance and stability of the antibody. This can be restored by adding an artificial peptide chain to the end of the antibody to restore J-chain binding ability. The peptide chain lacks the secondary structure encoding the sites that block secretion in native antibody heavy chains. Synthetic tailpieces (underlined) which are expected to work in transfected tobacco cells include:

(a) SCMVGHEALPMNFTQKTIDRLSGKPACY(SEQ ID NO: 7)

(b) SCMVGHEALPMNFTQKTIDRLSGKPAAACY(SEQ ID NO: 8)

(c) SCMVGHEALPMNFTQKTIDRLSGKPHASTPEPDPVACY(SEQ ID NO: 9) --

On page 25, line 6, please replace the original paragraph with the following amended paragraph:

-- Figures 9 and 10 show that using the -PAAAAACY (SEQ ID NO: 22) tailpiece as the C-terminus end of the heavy chain, whilst the efficiency of ennamer assembly of -PAAAAACY (SEQ ID NO: 22) is comparable to the wild-type IgA/G, recovery of -PAAAAACY (SEQ ID NO: 22) in the medium was 2.3-fold higher than wild-type IgA/G. --